Reviewer: Rick J. Whiting **Date: February 15, 2011**
Risk Manager (EPA): 23

STUDY TYPE: Acute Dermal Toxicity - Rat; OCSPP 870.1200; OECD 402

TEST MATERIAL: GF-2633 (Triisopropanolamine salt of Aminopyralid – 8.28 wt%; 2,4-D, dimethylamine salt – 42.2 wt%; Lot No. F1506-50, TSN032903-0001; pH: 7-8; soluble in water; clear liquid)

CITATION: Durando, J. (2010) GF-2633: Acute Dermal Toxicity Study in Rats. Project Number: 101014, 29303. Unpublished study prepared by Eurofins/Product Safety Laboratories. 30 p. July 1, 2010. MRID 48173004

SPONSOR: The Dow Chemical Company, Midland, MI 48674

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 48173004), young adult Fischer 344 rats (5/sex; age: 9-10 weeks; body weight: 225-240 g for males and 138-146 g for females; source: Harlan, Indianapolis, IN) were dermally exposed for 24 hours on an area of approximately 10% of the total body surface area on the clipped dorsal trunk to 5000 mg/kg of GF-2633 (Triisopropanolamine salt of Aminopyralid – 8.28 wt%; 2,4-D, dimethylamine salt – 42.2 wt%; Lot No. F1506-50, TSN032903-0001; pH: 7-8; soluble in water; clear liquid). The test material was applied evenly over the dose area of approximately 2 inches x 3 inches and covered with a gauze pad. The gauze pad and the entire trunk of each animal were wrapped with Durapore tape. After the exposure period, the pads were removed and the test sites were gently cleansed with a 3% soap solution followed by tap water and a clean paper towel to remove any residual test material. At the request of the Sponsor, the female rats were test first; due to the absence of mortality in these animals, the study proceeded with the male rats. Individual body weights were recorded prior to test material application and again on Days 7 and 14. Animals were observed for mortality, signs of gross toxicity and behavioral changes during the first hours after application and at least once daily thereafter for 14 days. Gross necropsies were performed on all animals.

All animals survived, gained body weight and appeared active and healthy during the study. Dermal irritation (erythema and edema) was noted at the dose site of all female rats and one male rat between Days 1 and 4. There were no other signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

Dermal LD_{50} Males > 5000 mg/kg bw
Dermal LD_{50} Females > 5000 mg/kg bw
Dermal LD_{50} Combined > 5000 mg/kg bw

Based on the LD_{50}, GF-2633 is classified as EPA Toxicity Category IV.

This acute dermal study is classified Acceptable. It does satisfy the guideline requirement for an acute dermal study (OCSPP 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

Statistics: The dermal LD_{50} was calculated using the limit dose.

A. Mortality: There were no deaths.

B. Body weights: All animals gained body weight during the study.

C. Clinical observations: All animals appeared active and healthy during the study. Dermal irritation (erythema and edema) was noted at the dose site of all female rats and one male rat between Days 1 and 4. There were no other signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior.

D. Gross Necropsy: No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

E. Reviewer's Conclusions: TRB agrees with the study author regarding the acute dermal LD_{50}. GF-2633 is classified as EPA Toxicity Category IV.

F. Deficiencies: None.